

WO 01/09187

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SEQUENCE LISTING

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<110> Medarex, Inc.

<120> HUMAN MONOCLONAL ANTIBODIES TO HER2/NEU

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<150> USSN 60/146,313
<151> 1999-07-29

<150> USSN 60/188,539
<151> 1999-03-10

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<170> PatentIn Ver. 2.0

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tcc ctg aga ctc tcc tgt gca gcc tct gga ttc acc ttt agc agc tat      96
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
      20              25              30

gcc atg acc tgg gtc cgc cag gct cca ggg aag ggg ctg gag tgg gtc
144
Ala Met Thr Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
      35              40              45

tca gct atc agt ggt agt ggt tat agc aca tac tac gca gac tcc gag
192
Ser Ala Ile Ser Gly Ser Gly Tyr Ser Thr Tyr Tyr Ala Asp Ser Glu
      50              55              60

aag ggc cgg ttc acc atc tcc aga gac aat tcc aag aac acg ctg tat
240
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
      65              70              75              80

ctg caa atg aac agc ctg aga gcc gag gac acg gcc gta tat tac tgt
288

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Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
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Ala Lys Gly Phe Gln Tyr Gly Ser Gly Ser Tyr Tyr Thr His Phe Asp
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Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120

<213> Homo sapiens

Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
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Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
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Ala Met Thr Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Ala Ile Ser Gly Ser Gly Tyr Ser Thr Tyr Tyr Ala Asp Ser Glu
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
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Ala Lys Gly Phe Gln Tyr Gly Ser Gly Ser Tyr Tyr Thr His Phe Asp
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Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
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<213> Homo sapiens

 $\langle 222 \rangle \quad (1) \dots (321)$

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gac aga gtc acc atc act tgt cgg gcg agt cag ggt att agc agc tgg 96
 Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Ser Ser Trp
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tta gcc tgg tat cag cag aaa cca gag aaa gcc cct aag tcc ctg atc
 144
 Leu Ala Trp Tyr Gln Gln Lys Pro Glu Lys Ala Pro Lys Ser Leu Ile
 35 40 45

tat gct gca tcc agt ttg caa agt ggg gtc cca tca agg ttc agc ggc
 192
 Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
 50 55 60

agt gga tct ggg aca gat ttc act ctc acc atc agc agc ctg cag cct
 240
 Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
 65 70 75 80

gaa gat ttt gca act tat tac tgc caa cag tat aat agt tac ccg tac
 288
 Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Asn Ser Tyr Pro Tyr
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<210> 4
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 <212> PRT
 <213> Homo sapiens

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 20 25 30

Leu Ala Trp Tyr Gln Gln Lys Pro Glu Lys Ala Pro Lys Ser Leu Ile
 35 40 45

Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
 50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
 65 70 75 80

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Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Asn Ser Tyr Pro Tyr
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Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
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<212> DNA

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<222> (1) .. (366)

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tcc ctg aga ctc tcc tgt gca gcg tct gga ttc acc ttc agt agc tat 96
 Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
 20 25 30

gac ata cac tgg gtc cgc cag gct cca ggc aag ggg ctg gag tgg gtg
 144
 Asp Ile His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
 35 40 45

gca gta ata tgg tat gat ggc agt aat aaa tac cat gca gac tcc gtg
 192
 Ala Val Ile Trp Tyr Asp Gly Ser Asn Lys Tyr His Ala Asp Ser Val
 50 55 60

aag ggc cga ttc acc atc tcc aga gac aat tcc aag aac acg ctg tat
 240
 Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
 65 70 75 80

ctg caa atg aac agt ctg aga gcc gag gac acg gct gtg tat tac tgt
 288
 Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
 85 90 95

gcg aga aac tat ggt ttg ggg agt tat tat aac tac ttt gac ttc tgg
 336
 Ala Arg Asn Tyr Gly Leu Gly Ser Tyr Tyr Asn Tyr Phe Asp Phe Trp
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 366
 Gly Gln Gly Thr Leu Val Thr Val Ser Ser
 115 120

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<210> 6
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 <212> PRT
 <213> Homo sapiens

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 35 40 45
 Ala Val Ile Trp Tyr Asp Gly Ser Asn Lys Tyr His Ala Asp Ser Val
 50 55 60
 Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
 65 70 75 80
 Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
 85 90 95
 Ala Arg Asn Tyr Gly Leu Gly Ser Tyr Tyr Asn Tyr Phe Asp Phe Trp
 100 105 110
 Gly Gln Gly Thr Leu Val Thr Val Ser Ser
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 <222> (1)..(321)

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 gac aga gtc acc atc act tgt cgg gcg agt cat ggt att agc agc tgg 96
 Asp Arg Val Thr Ile Thr Cys Arg Ala Ser His Gly Ile Ser Ser Trp
 20 25 30
 tta gcc tgg tat cag cag aaa cca gag aaa gcc cct aag tcc ctg atc
 144
 Leu Ala Trp Tyr Gln Gln Lys Pro Glu Lys Ala Pro Lys Ser Leu Ile
 35 40 45
 tat gct gca tcc agt ttg caa agt ggg gtc cca tca agg ttc agc ggc

- 6 -

192
Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

agt gga tct ggg aca gat ttc act ctc acc atc agc agc ctg cag cct
240
Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

gaa gat ttt gca act tat tac tgc caa cag tat aat agt tac ccg tac
288
Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Asn Ser Tyr Pro Tyr
85 90 95

act ttt ggc cag ggg acc aag ctg gag atc aaa
321
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100 105

<210> 8
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<213> Homo sapiens

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35 40 45

Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Asn Ser Tyr Pro Tyr
85 90 95

Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
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<222> (1) .. (366)

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 1 5 10 15

tcc ctg aga ctc tcc tgt gca gcg tct gga ttc acc ttc agt agc tat 96
 Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
 20 25 30

gtc atg cac tgg gtc cgc cag gct cca ggc aag ggg ctg gag tgg gtg
 144
 Val Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
 35 40 45

gca gtt ata tgg tat gat gga agt aat aaa tac tat gca gac tcc gtg
 192
 Ala Val Ile Trp Tyr Asp Gly Ser Asn Lys Tyr Tyr Ala Asp Ser Val
 50 55 60

aag ggc cga ttc acc atc tcc aga gac aat tcc aag aac acg ctg tat
 240
 Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
 65 70 75 80

ctg caa atg aac agc ctg aga gcc gag gac acg gct gtg tat tac tgt
 288
 Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
 85 90 95

gcg ctt atg gtt cgg gga ctt att ata acg ggg tac ttt gac tac tgg
 336
 Ala Leu Met Val Arg Gly Leu Ile Ile Thr Gly Tyr Phe Asp Tyr Trp
 100 105 110

ggc cag gga acc ctg gtc acc gtc tcc tca
 366
 Gly Gln Gly Thr Leu Val Thr Val Ser Ser
 115 120

<210> 10

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<212> PRT

<213> Homo sapiens

<400> 10

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 20 25 30

Val Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
 35 40 45

- 8 -

Ala Val Ile Trp Tyr Asp Gly Ser Asn Lys Tyr Tyr Ala Asp Ser Val
 50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
 65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
 85 90 95

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 100 105 110

Gly Gln Gly Thr Leu Val Thr Val Ser Ser
 115 120

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<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (1)..(324)

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 Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Tyr
 20 25 30

tta gcc tgg tac caa cag aaa cct ggc cag gct ccc agg ctg ctg atc
 144

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile
 35 40 45

tat gat gca tcc aac agg gcc act ggc atc cca gcc agg ttc agt ggc
 192

Tyr Asp Ala Ser Asn Arg Ala Thr Gly Ile Pro Ala Arg Phe Ser Gly
 50 55 60

agt ggg tct ggg aca gac ttc act ctg acc atc agc agc cta gag cct
 240

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Glu Pro
 65 70 75 80

gaa gat ttt gca gtt tat tac tgt cag cag cgt agc aac tgg cct ccg
 288

Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Arg Ser Asn Trp Pro Pro
 85 90 95

tac act ttt ggc cag ggg acc aag ctg gag atc aaa
 324

- 9 -

Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
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<210> 12
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 Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile
 35 40 45
 Tyr Asp Ala Ser Asn Arg Ala Thr Gly Ile Pro Ala Arg Phe Ser Gly
 50 55 60
 Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Glu Pro
 65 70 75 80
 Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Arg Ser Asn Trp Pro Pro
 85 90 95
 Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
 100 105

<210> 13
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 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Description of Artificial Sequence: cloning vector

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360

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420

gccctgcacc attatgttcc ggatctgcat cgcaggatgc tgctggctac cctgtggaac
480

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540

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600

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1080

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1440

- 11 -

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2100

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2340

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3120

ataaaaaatag gcgtatcacg aggcctttc gtcttcaag
3159